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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/697,233	10/30/2003	David B. Volkin	19698YCC	9156

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EXAMINER	
VOGEL, NANCY S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/697,233	VOLKIN ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 44-68 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 44-68 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 44-62 are pending in the case.

Priority

If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the

application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

This application repeats a substantial portion of prior Application No. 09/948,337, filed 9/7/01, and adds and claims additional disclosure not presented in the prior application. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should

applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Applicants have claimed priority to Application No. 09/948,337 in the first line of the specification, as required 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). However, applicants have incorrectly stated that the instant application is a Continuation of said 09/948,337. As set forth in the last office action in 09/948,337, mailed on 6/3/03, it was determined that applicants added new matter in their amendment to the claims filed 3/24/03, and therefore, the instant application, which retains those same amendments to the claims, is properly a Continuation-in-Part of parent application 09/948,337. The first line of the instant application should be amended to state this.

Specification

The use of trademarks [CHELEX, TEFLON, DESFERAL etc.] has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 44-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 44, 46, 48, 52, 53, 59, 61, 63, 65, 67, and by dependence, claims 45, 47, 49-51, 54-58, 60, 62, 64, 66 and 68, are vague and indefinite in the recitation of "substantially supercoiled plasmid DNA". The instant specification does not provide any definition of what is intended by "substantially supercoiled", and therefore the intended metes and bounds of the claimed subject matter cannot be determined.

Claims 44, 46, 48, and by dependence, claims 45, 47, 49-51, are vague and indefinite in the recitation of the term "at least one non-reducing scavenging agent...at a weight to volume concentration **up to about 3%**" [emphasis added]. The specification does not define what concentrations are encompassed by this phrase, and therefore the intended metes and bounds of the claims cannot be determined. It is noted that there is close prior art disclosing a similar concentration of non-reducing scavenging agent in a supercoiled plasmid formulation, and there is nothing in the specification, prior art, or prosecution history, to indicate what range of concentration is covered by the term "about".

Claims 59, 61, 63, 65 and 67, and by dependence, claims 60, 62, 64, 66, and 68 are vague and indefinite in the recitation of a method step of placing the plasmid DNA formulation into a second formulation and lyophilizing the solution. The introduction of a

method step in a composition claim raises the question of what is being claimed, i.e. a method or a composition. As a result, the claims are vague and indefinite. In the interest of compact prosecution, the claims have been examined as if they recited a lyophilized product comprising the recited plasmid DNA and an amorphous sugar.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 44-49 are rejected under 35 U.S.C. 102(b) as being anticipated by Maniatis et al. (Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory, 1982).

Maniatis et al. disclose a stabilized substantially supercoiled (i.e. closed circular form) plasmid DNA formulation comprising a buffered solution (TE) comprising Tris-HCl buffer and purified substantially supercoiled plasmid DNA, and the metal ion chelator EDTA at a concentration of 1mM (1000 uM) (see page 93-94). . It is noted that the

term "at a weight to volume concentration up to about 3%" recited in part (c) of the claims 44, 46, and 48, includes zero as a lower limit. *In re Mochel,* 470 F. 2d 638, 176 USPQ 194 (CCPA 1974) and MPEP Chapter 2171.

Claims 44-49 are rejected under 35 U.S.C. 102(e) as being anticipated by Michejda et al. (US Patent 5,672,593).

Michejda disclose a stabilized substantially supercoiled plasmid DNA formulation comprising a buffer which is Tris at 10 mM pH 7.4, a metal ion chelator which is EDTA at 0.1 mM (100 uM), and DMSO at a concentration of 5% see column 11, lines 34-44, and Fig. 6, lane 4). It is noted that the reference discloses that Figure 6 shows the results of a supercoiled plasmid strand break assay, in which 0.5 uL of a compound of interest dissolved in DMSO is added to 9.5 uL of plasmid DNA in TE buffer, resulting in a DMSO concentration of 5%, and the resultant plasmid DNA formulation is run on a gel. In the absence of a definition in the specification of the term "about 3%" set forth in part (c) of the claim, it is maintained that 5% would be encompassed by this term. It is noted that the amount of supercoiled form in lane 4 of Figure 6, is greater than half of the total intensity of plasmid DNA (supercoiled + open circle + linear) present in the lane, and therefore would be encompassed by the term "substantially supercoiled".

Claims 44-50 are rejected under 35 U.S.C. 102(e) as being anticipated by Niven et al. (US Patent No. 6,022,737).

Niven et al. disclose a substantially supercoilied plasmid DNA formulation comprising a buffered solution (Tris HCl), a metal ion chelator which is 1mM EDTA, and a salt which is NaCl (see column 6, lines 24-54). Note that the reference discloses eluting plasmid DNA from a column using the above buffer containing salt, and that supercoiled plasmid DNA is contained in certain fractions, as shown in Fig. 1 of the reference.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 44-49 and 59-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maniatis et al. (cited above) in view of Szoka et al. (WO 96/40265) Ulmer et al. (Science, Vol. 259, pp 1745-1749, 1993), and Content et al. (US Patent 5,736,524).

Maniatis et al. is cited essentially for the reasons set forth above.

The difference between the reference and the instant claims is that the DNA is present in lyophilized form, after being placed in a formulation comprising an amorphous sugar, and that the plasmid DNA encodes a viral or bacterial antigen DNA.

However, Szoka et al. teach formulations of DNA, including any plasmid DNA, which have been placed in a solution of amorphous sugar such as lactose and sucrose

and lyophilized. The reference teaches that the sugar stabilizes the plasmid DNA. The reference discloses that conventional buffers may be added to the mixture. The reference discloses that lyophilized forms of DNA such as plasmids are useful for long term storage prior to use (See abstract; see page 2 lines 5-14; see page 6 lines 4-7). Ulmer et al. teach plasmids encoding a viral antigen, such as influenza antigen (see abstract and pages 1745-1746); Content et al. teach plasmids encoding bacterial antigens, such as mycobacteria tuberculosis antigens, and viral antigens (see abstract, claim 1, column 3 line 3 – column 4, line 63).

It would have been obvious to one of ordinary skill in the art to have added a stabilizing sugar, as disclosed by Szoka et al, to a plasmid DNA, prepared by such standard procedures as that disclosed by Maniatis, in which Tris buffer and EDTA are present, in order to prepare lyophilized plasmid, since both references concern the formulations comprising plasmid DNA useful for storage or preservation of DNA preparations in undigested forms. One would have been motivated to do so by the increased stability of such preparations, as disclosed by Szoka et al., which discloses that lyophilization using preferentially sugars such as lactose and sucrose is useful for the long term storage of any plasmid DNA. Furthermore, it would have been obvious to have performed the same step of lyophilizing plasmid DNA which contained useful viral or bacterial antigen encoding genes, as taught by Ulmer et al. or Content et al., since these references teach the usefulness of such plasmids, and since Szoka et al. and Maniatis et al. teach plasmid formulations which are applicable to any plasmid of interest. Based upon the teachings of the cited references, the high skill of one of

ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

N. Vogel, Ph.D.
Patent Examiner